UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/380,276	08/27/99	TADA H	055555

HM22/0924

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EXAMINER	
O HARA, E	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/24/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/380,276	Applicant(s) TADA ET AL.	
	Examiner Eileen B. O'Hara	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *9 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-10* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in Paper No. 10 is acknowledged.

Claims 9 and 10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-8 are currently under examination.

Claim Objections

2. Claims 1, 2, 4 and 5 are objected to because of the following informalities:

2.1 Claims 1, 2, 4 and 5 recite a polypeptide of cDNA "that comprising" the amino-acid or nucleotide sequence, which is grammatically incorrect. The word "comprising" should be substituted with "comprises".

2.2 Claim 1 is also objected to because "A" should be inserted before "substantially" to be grammatically correct.

2.3 Claim 1 is also objected to because "or a" should be inserted after SEQ ID NO: 4 or 8," to be grammatically correct.

2.4 Claim 6 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n), *A.* for acceptable multiple dependent claim wording, and § 608.01(n), *B.* 1. For unacceptable multiple dependent claim wording. For example, that part of the claim could be rewritten as "--- the cDNA according to claims 3, 4 or 5

2.5 Claim 8 is also objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only, and cannot depend from any other multiple dependent claim. For unacceptable multiple dependent claim wording, see MPEP § 608.01(n) *B.* 3., for an example showing reference to two sets of claims to different features, and § 608.01(n) *B.* 4., for an example showing reference back to another multiple dependent claim.

Appropriate correction is required.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 1-8 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 1-8 are directed to isolated proteins comprising the amino acid sequences of SEQ ID NOS: 4 and 8, identified as OAFO65α and OAFO65β, respectively, and to nucleic acids encoding the proteins. The instant specification discloses that OAFO65α is a 417 amino acid protein, OAFO65β is a 423 amino acid protein, and that the first 415 amino acids of the two polypeptides are identical. The specification also provides sequence alignments with known tumor necrosis factor receptors (Fig. 1), and discloses that these two proteins are members of the tumor necrosis factor receptor family due to structural homology and the presence of conserved cysteine residues in the extracellular domain. Although the evidence is convincing that these polypeptides are probably receptors in the TNFR family, the proteins do not have any specific,

substantial and credible utility, as determined according to the current Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001.

Pages 17-35 of the instant application describe the uses and methods of the invention, and state that the nucleic acids and proteins can be used in methods such as therapies including administration of the proteins and gene therapy in diseases or disorders such as various immune deficiencies, use in regulating growth and proliferation of T and or B lymphocytes, use in treating infections including HIV, hepatitis, malaria, cancers, allergic reactions and conditions, chronic inflammation, regulation of myeloid or lymphoid cell deficiencies, transplantation, tissue regeneration including nerve and brain tissue, Alzheimer's, Parkinson's and Huntington's diseases, stroke, use as a contraceptive, use in suppressing or enhancing bodily characteristics such as height and eye color, use as an analgesic, use in treating depression and violent behaviors, use in correcting enzyme deficiencies, among many other proposed activities and treatments. The specification also teach that the proteins can be used to identify downstream signal transmission molecules which interact with them, to screen agonists/ antagonists and natural ligands, and the nucleic acids can be used to produce the encoded proteins and to screen for homologous genes.

However, these are not considered to be specific or substantial utilities for either the nucleic acid molecules or the proteins encoded by them. Methods such as identification of ligands or use to recombinantly produce protein are considered general methods applicable to any nucleic acid/protein, and are not considered specific or substantial. The assertion that the nucleic acids/and or proteins of the instant invention can be used in the treatment of diseases or disorders or to effect bodily change is also not a substantial utility, and is based on the

assumption that the proteins are receptors in the tumor necrosis factor receptor family, which as a family are involved in myriad biological pathways and activities. Many proteins are members of evolutionarily related families, yet have diverse biological activities and functions. Many proteins are members of evolutionarily related families, yet have diverse biological activities and functions. Skolnick et al. (Trends in Biotechnology, 2000) teach that because proteins can have similar structures but different functions, determining the structure of a protein may not necessarily reveal its function (see entire article, especially Box 2.). On page 34, right column, fifth paragraph down, Skolnick et al. States:

"In addition, proteins can gain and lose function during evolution and may, indeed, have multiple functions in the cell (Box 1). Sequence-to-function methods cannot specifically identify these complexities. Inaccurate use of sequence-to-function methods has led to significant function-annotation errors in the sequence databases[17]."

There is no nexus between any of the diseases or disorders and the molecules of the instant invention. Given no disease state or any other function or activity known for the proteins, the proteins are not considered to have utility. In Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct,.1966), a process of producing a novel compound that was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be useful because the compound produced thereby was potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The instant claims are drawn to a polynucleotide

encoding a protein which has undetermined function or biological significance, and the use of an orphan receptor to discover it ligand or properties does not constitute a specific, substantial utility. All of the biological activities of a protein need not be known to obtain a patent, but there must be some specific and substantial activity or function known. It is possible that after further characterization, this protein might be found to have a patentable utility, in which case the polynucleotides encoding the proteins would have a specific utility, or the polynucleotides might be found to be associated with a specific disease. This further characterization, however, is part of the act of invention, and until it has been undertaken the Applicants' claimed invention is incomplete. Because there is no specific and substantial utility asserted, credibility cannot be assessed.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4.1 Claims 1-8 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Even if the specification were enabling of how to use the DNA98853 polypeptide, enablement would not be found commensurate in scope with the claims. If one of skill in the art does not know how to use the proteins, the skilled artisan would clearly not know how to use homologues of the proteins or homologues of fragments of the proteins disclosed in the specification.

4.2 Claims 1 and 3-8 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification describes protein sequences consisting of SEQ ID NOs:4 and 8. However, the claims as written include polypeptides comprising homologues and homologues of fragments of the polypeptides, and encompass polypeptides that vary substantially in length and also in amino acid composition. The specification on page 5 defines a homologue as being at least 70% homologous to the polypeptide over a region of at least 20 amino acids. The instant disclosure of two highly homologous proteins (98.4% identical), does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, only two highly related polypeptides. Given the unpredictability of homology comparisons, and the fact that the specification fails to provide objective evidence that the additional claimed polypeptides are indeed species of the claimed genus, it cannot be established that a representative number of species have been disclosed to support the genus claim.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5.1 Claims 1-8 are vague and indefinite because they encompass a polypeptide, a homologue thereof, fragment thereof or homologue of the fragment. The specification on pages 5-6 defines a fragment of a polypeptide as being at least 10 amino acids in length, and a homologue at least 70% homologous over a region of at least 20 amino acids. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the broad recitation the polypeptide of SEQ ID NO: 4 or 8, and the claim also recites a homologue thereof, fragment thereof or homologue of the fragment, which is the narrower statement of the range/limitation.

5.2 Claims 4-8 are also indefinite because claims 4 and 5 encompasses a cDNA or a fragment cDNA selectively hybridized to the cDNA. The specification on page 6 defines a DNA "capable of selectively hybridizing to the DNA comprising nucleotide sequence shown in SEQ ID NO: 1, 2, 5 or 6 will be generally at least 70% ...homologous to the DNA comprising a nucleotide sequence shown in SEQ ID NO: 1, 2, 5 or 6 over a region of at least 20, ... Contiguous nucleotides." As in the rejection above, a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6.1 Claims 5, 6 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Takeda, Database EST, Accession No. D82546, Feb. 9, 1996.

Claims 5, 6 and 7 encompass a cDNA comprising a fragment of cDNA that selectively hybridizes to the nucleic acid of SEQ ID NO: 2 or 7, vector and host cell.

Takeda discloses a nucleic acid that is 100% identical to nucleotides 1540-1704 of SEQ ID NO: 2 (165 contiguous nucleotides), vector and host cell. Since the specification on page 6 defines a fragment of DNA as comprising at least 10 nucleotides, and defines a DNA capable of

selectively hybridizing to the DNA as 70% homologous to the DNA over a region of at least 20 contiguous nucleotides, the nucleic acid of Takeda meets the limitations of the claim. Thus, Takeda anticipates the claims.

6.2 Claims 3-7 are rejected under 35 U.S.C. 102(a) as being anticipated by Hillier et al., Database EST, Accession No. W56629, Oct. 15, 1996.

Claims 3-7 encompass a cDNA encoding a polypeptide or fragment of a polypeptide, or a cDNA comprising a fragment of cDNA that selectively hybridizes to the nucleic acid of SEQ ID NO: 1 or 5, vector and host cell.

Hillier et al. discloses a nucleic acid that is 99.7% identical to nucleotides 972-1269 of SEQ ID NO: 1 (298 contiguous nucleotides, encoding amino acids 285-383 of SEQ ID NO: 4), vector and host cell. Since the specification on page 6 defines a fragment of DNA as comprising at least 10 nucleotides, and defines a DNA capable of selectively hybridizing to the DNA as 70% homologous to the DNA over a region of at least 20 contiguous nucleotides, the nucleic acid of Hillier meets the limitations of the claims. Thus, Hillier anticipates the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Takeda, as applied to claims 5, 6 and 7, or Hillier, as applied to claims 3-7 above, and further in view of Sibson et al., WO 94/01548.

These claims encompass a polypeptide, homologue or fragment of a polypeptide and method for producing a polypeptide comprising culturing a host cell of claim 7 under conditions to express the polypeptide.

The teachings of Takeda and Hillier et al. are summarized as above. The cDNA of Hillier et al. encodes amino acids 285-383 of the polypeptide of SEQ ID NO: 4 (98 amino acids). The specification on pages 5-6 defines a fragment of a polypeptide as being at least 10 amino acids in length, and a homologue at least 70% homologous over a region of at least 20 amino acids. Takeda and Hillier et al. do not disclose a polypeptide or method for producing a polypeptide.

Sibson et al. disclose that it is generally useful to place a desired cDNA sequence into an expression vector and host cell and to express the encoded protein (see pages 8-13).

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use the cDNA of Takeda or Hillier et al. and host cell to express and then isolate the encoded polypeptide, as taught by Sibson et al. in view of Sibson et al.'s suggestion that it would be desirable to do so, as cited above. The skilled artisan would be motivated to do so in order to easily produce and analyze the encoded protein to determine its biological activity, and there would be a reasonable expectation of success, since this is a method that has been widely and successfully used in the field of molecular biology.

Conclusion

8. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242.

Informal papers filed by fax should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner

LORRAINE SPECTOR
PRIMARY EXAMINER